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(19)(CA) APPLICATION FOR CANADIAN PATENT (12)

(54) Method of Inactivation of Viral and Bacterial Blood Contaminants

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(US) 632,277 1990/12/20

(57) 90 Claims

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PATENT COOPERATION TREATY NA #2056619

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF LATE SUBMISSION OF APPLICATION NUMBER OF EARLIER APPLICATION

(PCT Administrative Instructions, Section 408(b) and (c))

To:

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Date of mailing (day/month/year) 12 October 1992 (12.10.92)		
Applicant's or agent's file reference 18024-0071		INFORMATION ONLY
International application No. PCT/US91/02504	International filing date (day/month/year) 16 April 1991 (16.04.91)	Priority date (day/month/year) 16 April 1990 (16.04.90) 20 December 1990 (20.12.90) 15 February 1991 (15.02.91)
Applicant		

1. The applicant is hereby notified that the application number of the earlier application, the priority of which is claimed in the international application, was furnished on:

   15 September 1992 (15.09.92)

2. This date occurs AFTER the expiration of 16 months from the priority date.

   [ ] and before technical preparations for international publication have been completed.

   Accordingly, the international publication of the international application will indicate that number and the fact that it was furnished late.

   [X] and after the technical preparations for international publication have been completed.

   Accordingly, the international publication of the international application indicated/will indicate that the number was not furnished. A copy of this notification will be sent to the designated Offices.

3. Where the priority of two or more earlier applications was claimed, this Notification relates to the following earlier application(s):

   US 15 February 1991 (15.02.91) 656,254

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INTERNATIONAL SEARCH REPORT

International Application PCT/US91/02504

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [6]

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC(5): A61K 35/14

U.S. CL.: 435/2; 424/529, 530, 531, 532, 533, 534

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
U.S.	435/2; 424/529, 530, 531, 532, 533, 534

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [8]

APS, CA Reg, CAS, BIOSIS

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category [10]	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No. [13]
Y	Vox Sang, Vol. 26, issued 1974 K. GANSHIRT ET AL., "A five-bag system for washing fresh and frozen erythrocytes and their preservation", pages 66-73, see page 66.	1-17
Y	Cryobiology, Vol. 10, issued 1973, D. PRIBOR, "Studies with Dextran 40 in cryopreservation of blood", pages 93-103, see entire article.	1-17
Y	Acta Vet Scand, Vol. 20, issued 1979, V. MYHRVOID, "Cryopreservation of sheep red blood cells", pages 531-536, see entire article.	1-17
Y	US, A, 4,874,690 (GOODRICH ET AL), 17 October 1989, see entire document.	1-17
X	US, A, 4,071,412 (EISENBERG ET AL.) 31 January 1978, see entire document.	1-17

(cont.)

* Special categories of cited documents [10]

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
09 July 1991	12 AUG 1991

International Searching Authority	Signature of Authorized Officer
ISA/US	Sandra Saucier (vsh)

Form PCT/ISA/210 (second sheet) (July 1989)

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510,234	16 April 1990 (16.04.90)	US
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(81) Designated States: AT (European patent), AU, BE (European patent), CA, CH (European patent), DE (European patent), DK (European patent), ES (European patent), FR (European patent), GB (European patent), GR (European patent), IT (European patent), JP, LU (European patent), NL (European patent), SE (European patent).

Published
With international search report.

(54) Title: METHOD OF INACTIVATION OF VIRAL AND BACTERIAL BLOOD CONTAMINANTS

(57) Abstract

A method is provided for inactivating viral and/or bacterial contamination in blood cellular matter, such as erythrocytes and platelets, or protein fractions. The cells or protein fractions are mixed with chemical sensitizers and irradiated with, for example, gamma or X-ray radiation.

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

V. ☐ OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE *

This international search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1 ☐ Claim numbers , because they relate to subject matter not required to be searched by this Authority, namely:

2 ☐ Claim numbers , because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3 ☐ Claim numbers _____, because they are dependent claims not drafted in accordance with the second and third sentences of PCT Rule 6.4(a).

VI ☒ OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING *

This International Searching Authority found multiple inventions in this international application as follows:

(See Attached Sheet)

1 ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.

2 ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:

3 ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:

4 ☐ As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remark on Protest

☐ The additional search fees were accompanied by applicant's protest.

☒ No protest accompanied the payment of additional search fees.

METHOD OF INACTIVATION OF VIRAL AND BACTERIAL BLOOD CONTAMINANTS

FIELD OF THE INVENTION

This invention relates to the general field of biochemistry and medical sciences, and specifically to inactivating viral/bacterial contamination of lyophilized or reconstituted blood cell compositions comprising erythrocytes, platelets, etc, or protein fractions.

BACKGROUND OF THE INVENTION

A major concern in the use of stored or donated homologous blood or plasma protein preparations derived from human blood is the possibility of viral and bacterial contamination.

Viral inactivation by stringent sterilization is not acceptable since this could also destroy the functional components of the blood, particularly the erythrocytes (red blood cells) and the labile plasma proteins. Viable RBC's can be characterized by one or more of the following: capability of synthesizing ATP; cell morphology; P_{50} values; oxyhemoglobin, methemoglobin and hemichrome values; MCV, MCH, and MCHC values; cell enzyme activity; and *in vivo* survival. Thus, if lyophilized then reconstituted

SUMMARY OF THE INVENTION

The present invention provides a method for viral/bacterial inactivation of dried or reconstituted cells (erythrocytes, platelets, hemosomes and other cellular or cell-like components) or blood protein fractions, which allows for the cells or protein fractions to be useful in a transfusable state, while still maintaining relatively high cell viability, ATP synthesis and oxygen transport, in the case of cellular components, and therapeutic efficacy, in the case of protein fractions.

The lyophilization and reconstitution media according to the present invention may be utilized to lyophilize and reconstitute proteins, particularly, blood plasma protein fractions. The protein fraction may be virally/bacterially deactivated by mixing with a chemical sensitizer, lyophilized (freeze-dried), then irradiated. If the lyophilization media of the invention is used, it is contemplated that the constituents of the media also serve to provide some degree of protection of the dry proteins during irradiation.

A preferred embodiment comprises reducing viral and bacterial contamination of dried or reconstituted cells with washing solutions containing a polymer or mixture of polymers having a molecular weight in the range of about 1K to 360 K, followed by one or more additional wash cycles using a wash of a dextrose-saline solution at a pH in the range of about 7.0-7.4. The dextrose-saline solution will also contain a polymer having a molecular weight in the range of about 1K t 40K, and preferably about 2.5K.

drying (the amount of residual moisture) is of critical importance in the ability of cells to withstand long-term storage at room temperature. Using the procedure described herein, cells may be lyophilized to a residual water content of less than 10 weight %, preferably less than 3%, and still be reconstituted to transfusable, therapeutically useful cells. Cells with about 3 weight % water content using this procedure may be stored for up to two weeks at room temperature, and at 4°C for longer than eight months, without decomposition. This far exceeds the current A.A.B.B. standard for refrigerated storage of red blood cells of six weeks at 4°C or less than one day at room temperature without decomposition. These dried cells may be deactivated using a chemical sensitizer described herein.

According to the preferred embodiment of the present invention the washed packed red blood cells are mixed with a chemical sensitizer, then washed to remove excess sensitizer not bound to viral or bacterial nucleic acid, and the treated cells are then lyophilized. The dry cell and sensitizer mixture will then be irradiated, typically with gamma radiation, at an intensity of about 3K-50K rads, for a period of time sufficient to destroy viruses (in particular, the single-stranded or double-stranded RNA/DNA viruses), without any substantial adverse effect on the recovery and usefulness of the cells. Other wavelengths of electromagnetic radiation such as X-rays, may be used.

In another preferred embodiment, the chemical sensitizers may be added to liquid protein

contamination. It is contemplated that liquid and frozen protein fractions may also be decontaminated according to the present invention.

Depending upon the nature of the presumed radiolytic mechanism of the sensitizer reaction with the virus, other types of radiation may be used, such as X-ray, provided the intensity and power utilized is sufficient to inactivate the viral contamination without adverse effect on the cells. Mature human red blood cells and platelets lack nucleic acids; therefore the nucleic acid binding sensitizers selectively target contaminating viruses and bacteria. Although described in connection with viruses, it will be understood that the methods of the present invention are generally also useful to any biological contaminant found in stored blood or blood products, including bacteria and blood-transmitted parasites.

DETAILED DESCRIPTION OF THE INVENTION

The cells are preferably prepared by immersing a plurality of erythrocytes, platelets and/or hemosomes, etc. in a physiologic buffered aqueous solution containing a carbohydrate, and one or more biologically compatible polymers, preferably having amphipathic properties. By the term amphipathic it is meant there are hydrophobic and hydrophilic portions on a single molecule. This immersion is followed by freezing the solution, and drying the frozen solution to yield novel freeze-dried erythrocytes containing less than 10%, and preferably about 3% or less by weight of moisture, which, when reconstituted, produce a significant percentage of viable, transfusably useful red blood cells,

The invention will be hereafter described in connection with erythrocytes (RBC's) but it will be understood it is also applicable to platelets, hemosomes or other blood cell types or biological cells, as well as protein fractions, particularly plasma protein fractions.

The erythrocytes will preferably be prepared from whole blood centrifugation, removal of the plasma supernatant and resuspending the cells in PBS or a phosphate buffered solution or a commercial dextrose-saline solution. This wash cycle may be repeated 2-3 times preferably using a commercial dextrose-saline solution, then the packed cells are diluted with the lyophilization buffer described above so that the final diluted concentration of carbohydrate and polymer are maintained in the necessary ranges.

Alternatively, commercially available packed blood cells may be used, which typically are prepared in CPDA (commercial solution containing citrate, phosphate, dextrose and adenine).

Upon lyophilization to a moisture content of less than 10%, and preferably less than 3%, the lyophilized cells may be maintained under vacuum in vacuum-tight containers, or under nitrogen or other inert gas, at room temperatures for extended periods of time in absence of or without significant degradation of their desirable properties when reconstituted for use as transfusable cells. In using the preferred lyophilization method disclosed herein, a particular advantage of the present invention is that the lyophilized cells may be stored at room temperature for extended periods of time,

adenosine triphosphate (ATP) in a final concentration of about 5mM.

The polymers may be present in the various solutions from a final concentration of about 3.6K weight % up to saturation, and have a molecular weight in the range of from about 2.5K to about 360K. Preferably, the polymers have molecular weights in the range of from about 2.5K to about 500K, most preferably from about 2.5K to 50K, and are present in a concentration of from about 3.6 weight % up to the limit of solubility of the polymer in the solution. Polymers selected from the group consisting of polyvinylpyrrolidone (PVP) and polyvinylpyrrolidone derivatives, and dextran and dextran derivatives provide significant advantages. Most preferred is the use of polyvinylpyrrolidone (an amphipathic polymer) of average molecular weight in the range of 2.5-360K in an amount in the range of 3-20% weight by volume in the solution prior to lyophilization. Amino acid based polymers (i.e., proteins), dextrans or hydroxyethyl starch may also be employed. In the lyophilization buffer hydroxyethyl starch (M-HES) with an average molecular weight of about 500K is employed in a 15% weight by volume final concentration. Other amphipathic polymers may be used, such as poloxamers in any of their various forms. The use of the carbohydrate-polymer solution in the lyophilization of red blood cells allows for the recovery of intact cells, a significant percentage of which contain biologically-active hemoglobin.

The most preferred reconstitution buffer will be a solution comprising monopotassium phosphate, disodium

acid, inosine, adenine, glutamine, and magnesium chloride, all present at about 0.4-10mM further comprising sodium chloride and potassium chloride each at about 30mM, buffered by 10mM disodium phosphate to pH 7.2. This wash buffer further comprises a monosaccharide, preferably glucose at a concentration of about 20mM, and a polymer, preferably polyvinylpyrroltidone, of a molecular weight 40K and present at a concentration of about 16% weight by volume. Separation by centrifugation completes the first post-rehydration step, a washing step.

After the washing step the rehydrated cells may be suspended in a dextrose-saline transfusion buffer at room temperature which preferably contains polyvinylpyrrolidone at a 10% weight by volume final concentration, with an average 2.5K molecular weight. The cells can be used as is or be returned to autologous plasma. Additional wash steps in a phosphate-buffered diluent buffer can further remove viruses, but this step is optional for preparation of rehydrated, transfusible cells.

The reconstitution and washings described above will in most instances achieve about 4 log reduction of any viral and bacterial contamination, where 1 log reduction is achieved by drying and 3 log reduction is achieved by washing. Of course, different viruses may respond differently, potentially resulting in more than 4 log reduction of contamination.

The reconstituted cells have characteristics which render them transfusable and useful for therapeutic

sensitizing and treatment, particularly while the cells or protein fractions are in the dry state.

The starting packed red blood cells or proteins (which may initially be in a liquid or lyophilized state) are mixed with a sufficient amount (based on total wet weight of cells) of a chemical sensitizer. Preferably, in a composition of packed red blood cells (about 10% hematocrit) about 0.1 to 1 mg of the chemical sensitizer will be used per ml of packed cells. Preferably, the mixture will be irradiated with gamma radiation in the range of 3K-50K rads, typically about 3K rads. Preferred exposure is from 1-10 minutes, if using gamma radiation. Alternatively, UV light (320 nm) may be used, particularly for protein fractions. Preferred exposure is from 1-10 minutes, preferably 3 minutes, if using UV radiation. By this irradiation in presence of a sensitizer, there will be about a 6 log reduction of viral and bacterial contamination, based on contamination present prior to washing and irradiation.

The present invention provides a selective method of generating free radicals derived from chemical sensitizers only in the vicinity of viral RNA or DNA. Indiscriminate radiolysis of blood containing virus in a hydrated state produces hydroxyl radical. However, the hydroxyl radical will damage both the red blood cells and associated proteins as well as the viral target. Thus, viral inactivation would be achieved at the sacrifice of red cell viability. Therefore, sensitizers which bind to DNA and/or RNA and which can be selected to generate radicals upon irradiation, are required. Since the radiolysis can

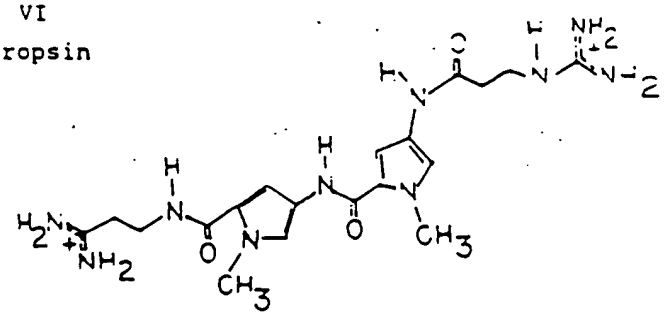
disclosed in Pjura, P.E., Grzeskowiak, K. and Dickerson, R.E. (1987), J. Mol. Biol., 197, 257-271 and Teng, M., Usman, N., Frederick, C.A. and Wang, A.H.J. (1988), Nucleic Acids Res. 16, 2671-2690.

The radiation sensitizing compound (which may also bear a metal atom) can also comprise a class of DNA-binding proteins and/or polypeptides and/or peptides. Examples of this class of DNA-binding proteins and/or polypeptides and/or peptides are disclosed in Churchill, M.E.A. and Travers, A.A. (1991) Trends in Biochemical Sciences 16, 92-97. Specific examples of DNA-binding peptides include the SE peptide and BD peptide disclosed in the reference herein.

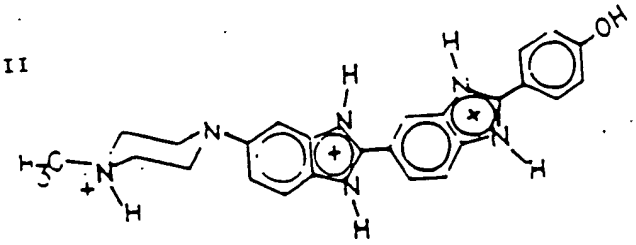
The DNA-binding specificity can be achieved by covalently coupling the radiation sensitizing compound and/or metal atom to either a DNA-binding drug or to a DNA-binding protein or polypeptide or peptide.

VI

Netropsin



VII



removed during the washing steps involved in the reconstitution of the lyophilized cells (Table 2). This process will also further remove any virus not inactivated by the treatment described above.

Compounds (1) and (2) bind tightly to DNA and RNA by either intercalation and/or by electrostatic interactions between positively charged ammonium ion groups and the negatively charged phosphate groups of the nucleic acid target. Red blood cells do not contain nucleic acids and accordingly will not bind to such compounds by intercalation.

The best mode for using the invention is to add the sensitizer to potentially contaminated blood solutions, and to expose to gamma radiation or x-rays. Fluid solutions of blood are preferably exposed to 3000 rads, and dried lyophilized solid formulations are preferably exposed to 10,000 rads of radiation. It is known that the red cells will survive these doses of radiation in the absence of a sensitizer. Lyophilized blood can withstand higher dosage levels of radiation than hydrated blood.

The gamma radiation or x-ray will be absorbed primarily by the heavy atom of the sensitizer, which will be bound to viral DNA or RNA. The radiation will ionize the sensitizer as follows:

$$R\text{-}I + \gamma\text{-Ray} \text{ (X-Ray)} \rightarrow R\text{-}I^{**} + e^{-}$$

In some instances, particularly if the sensitizer and red blood cells are allowed to stand together for more than several minutes, sensitizers may diffuse into the red blood cells prior to lyophilization.

means to remove unreacted material or reaction by-products, and further removes any virus not affected by the treatment (Table 2).

Other types of radiation may be used including ionizing radiation in general, such as X-ray radiation. In one embodiment a metal atom may be a substituent on a chemical radiation sensitizer molecule which binds to nucleic acids, thereby targeting the embodiments such as bacteria, parasites and viruses. Metal atom substituents of chemical sensitizers for this purpose include Br, I, Zn, Cl, Ca and F. The X-ray source is preferably a tunable source, so that the radiation may be confined to a narrow wavelength and energy band, if so desired. The tunable feature allows for optimization of energy absorption by the metal atoms, thereby directing the absorbed penetrating radiation energy to the production of radicals by a chemical sensitizer bound to nucleic acid.

The present invention is applicable to contaminants which comprise single or double-stranded nucleic acid chains, including RNA and DNA, and viruses, bacteria or other parasites comprising RNA and/or DNA.

To illustrate the invention, red blood cells were lyophilized as described above, irradiated, and tested for erythrocyte characteristics measured. The results are shown in Table 1. The same procedure was then used, except that the bacteriophage T4 (in dextrose saline) was mixed with the cells and then washed successively with four different wash buffers. The results are shown in Table 2.

Table 2: Reduction in viral titre as a function of washing of the red cells. The procedure used in reconstituting the lyophilized cells involves several washing steps which also reduce the viral titre. The extent of reduction with each wash decreases until a practical limit is attained. This represents an approximate 4 log reduction in viral titre.

Washing Protocol Reduction of Viral Load in Blood

Buffer Wash Step	Total Amount of Virus	Log Reduction
Experiment 1 (non-lyophilized cells)		
Reconstitution	$7.3\ 0x\ 10^7$	0
Wash	4.80×10^4	3.2
Diluent	2.08×10^4	3.5
Transfusion	3.50×10^4	3.3
Experiment 2 (lyophilized cells)		
Lyophilization	3.68 x 108	0
Reconstitution	2.11 x 107	1.2**
Wash	2.38 x 104	4.2
Diluent	2.00 x 104	4.3
Transfusion	4.06 x 104	4.0

In Experiment 1, the effects of lyophilization on viral reduction are not included. In Experiment 2, these effects are included. The marker virus used in these cases was bacteriophage T4. The extent of reduction was determined using the plaque assay.

**This shows an additional about 1 log reduction of contamination due to the drying step.

An exposure of 3 minutes was judged to be usable for viral inactivation using a radiation sensitizer, without inflicting excessive damage to red blood cells.

EXPOSURE (Minutes)	% OXYHB	% METHB	% HEMI
0	96.6	3.4	0
2	90.2	7.5	2.3
4	84.5	13.4	2.1
6	76.7	22.5	0.9
8	72.6	27.4	0
10	66.4	33.6	0

EXAMPLE 2

A suspension (0.1 ml) of bacteriophage lambda or bacteriophage phi-X174, of at least 10EV PFU/ml, is separately added to 4 ml of dextrose-saline containing 1 mg/ml of compounds I or II or III. Each suspension of bacteriophage with a radiation sensitizing compound is then exposed to U.V. radiation of the preferred wavelength (320 nm) in a quartz chamber for the preferred time (3 minutes). A control sample of each bacteriophage suspension, containing a sensitizer, is not exposed to U.V. light. Serial dilutions are performed to quantitate the level of infectious titer, and aliquots of the various bacteriophage samples are then mixed with host bacteria and spread on nutrient agar. Following a normal growth period, the plates are assayed for plaques. Other bacteriophage suspensions are separately irradiated as above, but without added sensitizer, to demonstrate the effect of this dose of U.V. alone.

WHAT IS CLAIMED IS:

1. A process of reducing viral and/or bacterial contamination in a dried or reconstituted composition comprising red blood cells, platelets, and/or proteins comprising:

mixing said composition with a sufficient volume of a phosphate-buffered reconstitution solution to form a mixture, wherein said reconstitution solution has a pH in the range of about 7.0-7.4 at a temperature in the range of about 15-50°C, said reconstitution solution further comprising a final concentration of about 0.7% by weight up to the saturation concentration of a polymer or mixture of polymers having a molecular weight in the range of about 1K to 360K,

separating said red blood cells, platelets and/or proteins from said mixture by centrifugation and washing by at least one wash cycle by resuspending said red blood cells, platelets and/or proteins in a dextrose-polymer wash buffer solution at a pH in the range of about 7.0-7.4 and separating by centrifugation to produce substantially decontaminated red blood cells, platelets and/or proteins.

2. A process according to Claim 1 further comprising the step of freeze-drying said decontaminated red blood cells, platelets and/or proteins.

3. A process according to Claim 1 or 2 wherein said polymers are amphipathic.

the group consisting of compounds which bind to DNA and/or RNA and are capable of selectively generating free radicals upon exposure to radiation, and exposing said composition to radiation of sufficient wavelength and intensity for a period of time sufficient to cause said sensitizer to further reduce viral and bacterial contamination in said composition.

13. A process according to Claim 12 wherein said composition comprises red blood cells.

14. A process according to Claim 12 wherein said composition comprises platelets.

15. A process according to Claim 12 wherein said composition comprises blood plasma proteins.

16. A process according to Claim 12 wherein said radiation comprises gamma radiation.

17. A process according to Claim 12 wherein said contamination comprises single- and/or double-stranded-type viruses.

18. A process for reducing viral and/or bacterial contaminations in a protein composition comprising the steps of contacting said composition with at least one chemical sensitizer selected from the group consisting of compounds which bind to DNA and/or RNA and are capable of selectively generating free radicals upon exposure to radiation, and exposing said composition to radiation of sufficient wavelength and intensity for a period of time sufficient to cause said sensitizer to further reduce

29. A substantially virally and bacterially decontaminated lyophilized composition comprising red blood cells, platelets and/or proteins, said decontamination resulting from exposure to electromagnetic radiation of sufficient wavelength and intensity to inactivate viral and bacterial contamination in said composition.

30. A substantially virally and bacterially decontaminated lyophilized composition comprising red blood cells, platelets and/or proteins and containing inactive viral and/or bacterial contaminants which have been deactivated by binding of the viral and/or bacterial DNA or RNA to at least one chemical sensitizer capable of selectively generating free radicals upon exposure to electromagnetic radiation, and by exposing said bound sensitizer to electromagnetic radiation of sufficient wavelength and intensity and for a period of time sufficient to cause said sensitizer to deactivate said RNA and/or DNA.

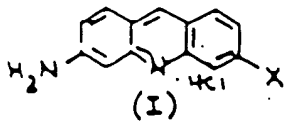
31. A composition according to Claim 29 or 30 comprising platelets.

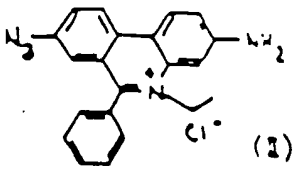
32. A composition according to Claim 29 or 30 comprising red blood cells.

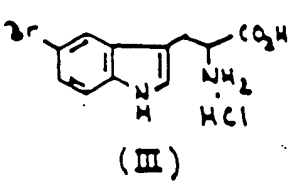
33. A composition according to Claim 29 or 30 comprising blood proteins.

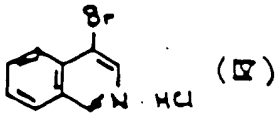
34. A composition according to Claim 33 comprising a clotting factor.

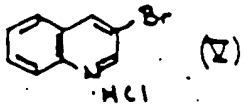
compounds of the formulas:











exposing said cellular matter to radiation of sufficient wavelength and intensity for a period of time sufficient to cause said sensitizer to substantially reduce viral and bacterial contamination in said blood cellular matter.

44. A method according to Claim 43 wherein said cellular matter comprises erythrocytes.

45. A method according to Claim 43 wherein said cellular matter comprises platelets.

46. A method according to Claim 43 wherein said radiation comprises ultraviolet radiation.

47. A method according to Claim 43 wherein said contamination comprises single- and/or double-stranded-type viruses.

53. A process according to Claim 1 or 2 wherein said radiation sensitizing compound comprises a metal atom.

54. A process according to Claim 53 wherein said metal atom comprises Br.

55. A process according to Claim 53 wherein said metal atom comprises I.

56. A process according to Claim 53 wherein said metal atom comprises Zn.

57. A process according to Claim 53 wherein said metal atom comprises Cl.

58. A process according to Claim 53 wherein said metal atom comprises Ca.

59. A process according to Claim 53 wherein said metal atom comprises F.

60. A method according to Claim 51 wherein said compound is sensitized by penetrating, ionizing radiation.

61. A method according to Claim 51 wherein said compound is sensitized by gamma radiation or X-rays.

62. A method according to Claim 52 wherein said radiation-sensitizing compound binds RNA.

63. A method according to Claim 52 wherein said radiation-sensitizing compound binds DNA.

monoclonal antibody or polyclonal antibodies directed against viral, bacterial and/or parasitic antigens.

72. A method according to Claim 71 wherein said radiation-sensitizing compound comprises a metal atom.

73. A method according to Claims 71 or 72 wherein said radiation sensitizing compound is activated by penetrating, ionizing radiation.

74. A method according to Claim 73 wherein said radiation comprises gamma radiation or X-rays.

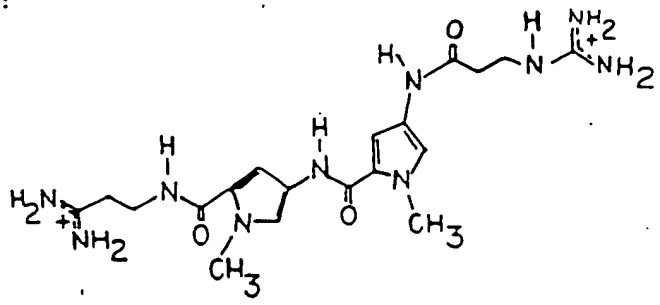
75. A method according to Claim 71 wherein said antigens comprise viral surface epitopes or viral envelope proteins.

76. A method according to Claim 71 wherein said antigens comprise bacterial surface epitopes.

77. A method according to Claim 71 wherein said antigens comprise surface epitopes of blood-transmitted parasites.

78. A method according to Claim 12 or 18 wherein said sensitizer comprises DNA-binding drugs.

79. A method according to Claim 78 wherein said DNA-binding drug comprises a compound of the formula VI:



86. A method according to Claim 84 wherein said DNA-binding protein, polypeptide, or peptide contains a metal atom substituent.

87. A method according to Claim 84 wherein said DNA-binding protein, polypeptide, and/or peptide is activated by ionizing penetrating radiation.

88. A method according to Claim 87 wherein said ionizing radiation comprises gamma radiation or X-rays.

89. A composition comprising cellular blood matter or blood proteins in which viral, bacterial, or parasitic contaminants have been substantially inactivated according to the method of Claim 78.

90. A composition comprising cellular blood matter or blood proteins in which viral, bacterial, or parasitic contaminants have been substantially inactivated according to the method of Claim 84.